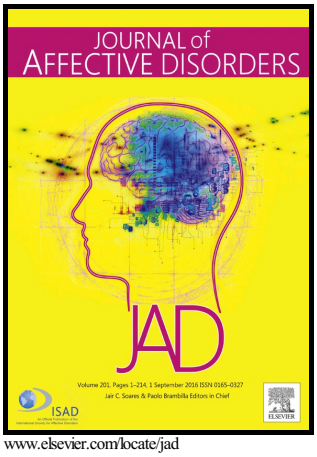


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# The effectiveness of adjunct mindfulness-based intervention in treatment of bipolar disorder: a systematic review and meta-analysis

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**Abstract:**

**Background:**

Mindfulness-based interventions (MBIs) have been increasingly used as an

adjunctive treatment to pharmacotherapy for a few psychiatric disorders. However, few studies have investigated the efficacy of MBIs in bipolar disorder (BD).

**Methods:**

We performed a systematic review and meta-analysis to evaluate the efficacy of MBIs **as an adjunctive treatment** in BD. Major electronic databases were independently searched by two authors for controlled and uncontrolled studies which examined the effects of MBIs on psychiatric symptoms in subjects with BD. Data from original studies were synthesized by using a random effects model.

**Results:**

Twelve trials were eligible for inclusion into current meta-analysis, including three controlled studies (n=132) and nine uncontrolled studies (n=142). In within-group analysis, MBIs significantly reduced depressive (7 studies, n=100, Hedges' *g*=0.58, p<0.001) and anxiety (4 studies, n=68, Hedges' *g*=0.34, p=0.043) symptoms, but not manic symptoms (6 studies, n=89, Hedges' *g*=0.09, p=0.488) and cognition (3 studies, n=43, Hedges' *g*=0.35, p=0.171), compared to baseline. In between-group analysis (intervention group versus waiting list group, all patients with BD), MBIs did not reduce depressive (3 studies, n=132, Hedges' *g*=0.46, p=0.315) or anxiety (3 studies, n=132, Hedges' *g*=0.33, p=0.578) symptoms.

**Limitations:**

Only three controlled trials compared MBIs to control conditions.

**Conclusions:**

Our meta-analysis showed significantly beneficial effects on depressive and anxiety symptoms of BD patients in within-group analysis. However, this significance was not observed in comparison with the control groups. Further clinical trials are warranted to investigate the differences in the benefits of MBIs between treatment and control subjects.

**Keywords:** psychiatry; adjunctive treatment; mindfulness; cognitive behavioral therapy

**Abbreviation list**

BAI: Beck anxiety index; BD: bipolar disorder; BDI: Beck depression inventory; CPAS: clinical positive affective scale; DASS: depression anxiety stress scales; DSM-IV: diagnostic and statistical manual of mental disorders, 4th edition; FFMQ: five-facet mindfulness questionnaire; HADS: hospital anxiety and depression scale; HAMD: Hamilton depressive scale; KIMS: Kentucky inventory of mindfulness skills, MAAS: mindful attention awareness scale; MADRS: Montgomery–Åsberg depression rating scale; MBI: mindfulness-based intervention; n/a: not available; Pre-post Tx: comparison of disease severity before and after treatment; STAI: state-trait anxiety inventory; TAU: treatment as usual; Tx: treatment; YMRS: Young mania rating scale



**Introduction**

The global prevalence of bipolar disorder (BD) in primary care is 1.8% (Stubbs et al., 2016), and it is one of the leading causes of disability worldwide (Garland et al., 2016). BD is characterized primarily by recurring affective episodes of depression, (hypo)mania and mixed states. In addition, patients with BD often have impaired psychosocial functions, even when in remission (Garland et al., 2016). Even after drug treatment, up to 48.5% of patients with BD have been reported to experience relapses and/or recurrence of major affective episodes within a 2-year follow-up

period (Perlis et al., 2006). Furthermore, even if these patients improve after acute episodes, pervasive depressive symptoms remain (Judd et al., 2003) in addition to the cognitive symptom of **emotional regulation disability** (Gruber, 2011). Several psychosocial interventions including interpersonal therapy, family therapy, and cognitive-behavioral therapy have been developed as adjunctive therapy to treat BD (Grande et al., 2016). Among these psychosocial interventions, psychoeducation, interpersonal therapy, family therapy, non-mindfulness based cognitive-behavioral therapy, and systematic care have been proven to be effective in preventing relapses, stabilizing episodes, and reducing episode length (Miklowitz, 2008; Miziou et al., 2015; Oud et al., 2016). For example, a recent meta-analysis by Oud et al reported that individual psychological interventions could reduce the severity of depressive but not manic symptoms (standardized mean difference [SMD] = -0.23, 95% confidence interval [CI] = -0.41 to 0.05; SMD = -0.05, 95% CI = -0.35 to 0.25, respectively). Another study also suggested that these non-medical therapies could help in ameliorating core inter-episode symptoms (Opialla et al., 2015).

Recently, interest has grown in the potential of mindfulness-based interventions (MBIs) to improve outcomes of patients with psychiatric illnesses. MBIs are based on the premise of paying total attention **on purpose** in the present moment and non-judgmental attention to inner and outer experiences moment by moment (Kabat-Zinn, 1994). MBIs were first developed by Kabat-Zinn as mindfulness-based stress reduction (MBSR) in the 1970s to enhance the stress coping skills of patients with chronic pain (Kabat-Zinn, 1990). Later, MBIs were used as the core of mindfulness-based cognitive therapy (MBCT) by combining elements of MBSR and cognitive therapy in order to prevent relapses/recurrence of unipolar depressive episodes (Teasdale et al., 1995; Teasdale et al., 2000). For example, a recent

meta-analysis which synthesized available evidence from 1,329 participants found that MBCT reduced depressive relapse rates within a 60-week follow-up period compared to participants who did not receive MBCT (Kuyken et al., 2016). Another meta-analysis suggested that MBIs could also be effective as an adjunctive treatment for negative symptoms among patients with psychosis (Khoury et al., 2013).

However, relatively few studies have investigated the effect of MBIs on treatment outcomes in patients with BD. Uncontrolled (Biseul et al., 2016; Bos et al., 2014; Crane et al., 2008; Deckersbach et al., 2012; Howells et al., 2014; Miklowitz et al., 2009; Miklowitz et al., 2015; Murray et al., 2015; Perich et al., 2013a; Stange et al., 2011; Weber et al., 2010) and controlled trials (Ives-Deliperi et al., 2013; Perich et al., 2013b; Van Dijk et al., 2013; Williams et al., 2008) have shown that the combination of MBIs with pharmacotherapy and treatment as usual (TAU) can have beneficial effects for patients with BD. Furthermore, a previous functional magnetic resonance imaging study showed the potential involvement and beneficial effects of MBIs in specific neural circuits underlying emotional regulation (Opialla et al., 2015), which is one of the main core inter-episode symptoms in BD (Gruber, 2011). Conversely, other studies have found no significant effect of MBIs on depressive (Howells et al., 2014; Ives-Deliperi et al., 2013; Perich et al., 2013b; Weber et al., 2010), manic (Deckersbach et al., 2012; Perich et al., 2013b), or anxiety (Howells et al., 2014) symptoms.

These inconsistencies may be due to the small sample size in most studies (Crane et al., 2008; Deckersbach et al., 2012; Miklowitz et al., 2009; Murray et al., 2015; Perich et al., 2013a; Stange et al., 2011; Van Dijk et al., 2013; Williams et al., 2008), lack of standardized outcome measurement, different intervention characteristics

(e.g. study duration varying from 3 to 12 weeks of MBCT training), different characteristics of the participants (Bos et al., 2014; Weber et al., 2010; Williams et al., 2008), high attrition rates early in the study (Bos et al., 2014; Murray et al., 2015), and disparate study designs (Bos et al., 2014; Howells et al., 2014; Murray et al., 2015; Van Dijk et al., 2013). In addition, the absence of a comparison treatment control group in many studies makes the findings less robust when considered in isolation (Bos et al., 2014; Crane et al., 2008; Deckersbach et al., 2012; Miklowitz et al., 2009; Murray et al., 2015; Stange et al., 2011; Weber et al., 2010).

Two meta-analyses investigating MBIs in patients with mental disorders have previously been conducted with mixed groups of patients with mood or anxiety disorders (Chiesa and Serretti, 2011; Hofmann et al., 2010). Whilst helpful, the generic focus, the fact that only two trials involving participants with BD were included, and failure to consider core symptoms of BD such as mania (Chiesa and Serretti, 2011), limits the conclusions regarding the efficacy of MBIs in patients with BD. More recently, several uncontrolled clinical trials examined the effectiveness of MBIs in patients with BD (Biseul et al., 2016; Bos et al., 2014; Miklowitz et al., 2015; Murray et al., 2015), however no dedicated systematic review and meta-analysis has investigated the use of MBIs as treatment for BD.

Given these limitations and gaps in the literature, we conducted this comprehensive systematic review and meta-analysis to investigate the role of MBIs as an adjunctive therapy for patients with BD.

**Method and Materials**

The current systematic review and meta-analysis was conducted in line with the

PRISMA guidelines (Liberati et al., 2009) (Supplement Table 1 and Supplement Figure 1).

**Eligibility criteria**

In order to be eligible for inclusion, articles had to meet the following criteria: (1) peer-reviewed original articles investigating the adjunctive effect of MBIs in patients with BD compared to a control group (controlled studies) or without a control group (uncontrolled studies); (2) a diagnosis of BD based on either DSM-IV (Association, 1994) or ICD (Diseases) code; (3) used MBIs (including MBSR, MBCT, and **other interventions** in which mindfulness represented a core component); and (4) articles written in English.

**We excluded non-clinical trials articles from the present study (e.g. case series, observational studies).** We also excluded studies investigating mixed populations of patients (e.g. both patients with BD and major depression joined), unless the articles provided separated data for those with BD and major depression. In addition, we excluded studies that examined mindfulness as part of another treatment modality as it would have been difficult to differentiate the treatment effect of mindfulness from other components (Khoury et al., 2013). Therefore, we excluded studies on dialectical behavior therapy and acceptance and commitment therapy. We also excluded studies with a short duration (< 3 weeks) and those on self-help interventions such as **online MBIs** (Murray et al., 2015)

**Database searches and study selection**

Two authors (CS Chu and PT Tseng) independently searched PubMed, ScienceDirect, EBSCOhost-Medline, Psychology and Behavior Sciences Collection, Cochrane library, and ClinicalTrials.gov from inception until November 28, 2016 using the following search terms: **(mindfulness OR meditation) AND (bipolar OR bipolar disorder).** A filter of "patient/treatment/mental health/depression/sleep/eeg/ptsd/anxiety/mental/bipolar disorder/participant/adhd/bipolar/anxiety disorder/emotion regulation/journal" were done on the platform of ScienceDirect (http://www.sciencedirect.com). Furthermore, potentially relevant studies were also identified from the reference lists of the included studies, reviews, and meta-analyses of interventions that used MBIs as adjunctive therapy to treat patients with BD (Chiesa and Serretti, 2011; Marchand, 2012; Mehrmann and Karmacharya, 2013; Sipe and Eisendrath, 2012).

Duplicates were removed from the total number of identified records. Abstracts from the remaining records were then screened to retrieve full-text articles to assess their eligibility. Full details of the search strategy are shown in Figure 1.

Following the database search, two authors independently screened the titles and abstracts of the search results to assess whether they met the inclusion criteria. The two authors selected a list of studies that met the eligibility criteria to be considered at the full text review. Any inconsistencies were resolved by consensus.

**Methodological quality appraisal**

Two independent authors rated the quality of the included articles using the Jadad scale (Jadad et al., 1996). The Jadad scale consists of a three-point questionnaire to assess the study with regards to it being randomized, double-blind, and whether it included a description of withdrawals and dropouts. Each question was answered with either yes or no, with a total score ranging from zero (poor quality) to five (high quality) (Supplementary Table 3).

**Primary outcomes**

The primary outcome was changes in scores from baseline to post-treatment in forms of standard rating scales assessing depressive, anxiety and manic symptoms. **The primary outcome was analyzed from 12 articles, four of them provided relevant data of intent-to-treat analysis** (Bos et al., 2014; Deckersbach et al., 2012; Miklowitz et al., 2015; Perich et al., 2013b).

**Secondary outcomes**

The secondary outcomes included the effect of MBIs on cognition, stress, emotional regulation, and mindfulness ability. In addition, we assessed the effect of MBIs on cognitive subdomains including attention, cognitive flexibility, executive, impulsiveness/distractibility, and spatial/verbal memory.

**Data extraction and management**

Two independent authors extracted data for the meta-analysis using a pre-specified data extraction form. These data included mean age, female gender, marriage, occupation, age at disease onset, disengagement early from the study, combined with other psychotherapy, and the use of alcohol/illicit drugs. Other variables related to MBIs included duration of mindfulness treatment, total number of sessions and duration of each session.

We also extracted data on the levels of depressive/manic symptoms/cognitive impairment according to the most commonly used scales in the included studies. The Beck depression inventory (BDI) was the most frequently used scale to assess depressive mood, followed by the depression anxiety stress scale (DASS) and Montgomery-Åsberg depression rating scale (MADRS). Therefore, we extracted the BDI scores of the participants with depression first, and then those of the DASS and MADRS. For anxiety, the scales were Beck anxiety index, DASS, and state-trait anxiety inventory (STAI), and for mania, the Young mania rating scale (YMRS). When data were not available in the articles, we attempted to contact the authors to ask for access to the data on at least two separate occasions.

**Meta-analysis**

The analyses included both controlled and uncontrolled studies **for between-group analysis and within-group analysis, respectively.** All meta-analytic procedures were performed using Comprehensive Meta-Analysis software, version 2 (Biostat, Englewood, NJ). For the primary and secondary outcomes, we calculated Hedges' *g* statistic as the estimate of within-group effect size (ES; and 95% confidence intervals (CIs)) for changes from pre-treatment to post-treatment **and between-group (intervention group versus control group) effect size** for each

outcome (depressive symptoms, anxiety, mania, stress, emotional regulation, cognition, and mindfulness ability). The Hedges' *g* statistic provides a relatively unbiased standardized ES estimate (Hedges and Olkin, 1985). We calculated the Hedges' *g* statistic with 95% CIs to compare the effect of MBIs in the controlled studies only. The Hedges' *g* statistics for the primary and secondary outcomes were calculated based on changes from baseline to post-test. **Some studies provide follow-up data (at 1, 3, 6, and 12 months after the MBIs), but we did not analysis these data in the present study (Deckersbach et al., 2012; Miklowitz et al., 2015; Perich et al., 2013a; Perich et al., 2013b; Stange et al., 2011; Weber et al., 2010).**

We next calculated the Hedges' *g* from baseline to post-treatment for MBIs across secondary outcomes including cognition scores and subdomains. In addition, where possible we performed subgroup meta-analysis if data from three or more **enrolled studies** were available. If Hedges' *g* could not be derived from the raw scores of each rating scale, we tried to derive Hedges' *g* from other statistical parameters such as the t or *p* value considering the sample size. Due to the anticipated heterogeneity, we employed a random-effects model for every meta-analysis in the current study. Subgroup analyses were conducted separating the included studies into uncontrolled and controlled studies.

We set statistical significance as two-tailed P values less than 0.05. We used the $I^2$ statistic and Cochran's Q test to examine heterogeneity across the included studies (Higgins et al., 2003). Heterogeneity was considered large when the *p* value of the Q test was less than 0.05. Publication bias was assessed through the visual inspection of funnel plots and with Egger's regression test (Egger et al., 1997). In addition, to investigate the possible confounding effects of clinical variables, we conducted

meta-regression and subgroup meta-analyses. The meta-regression procedure was performed with an unrestricted maximum likelihood method only if five studies were available, and subgroup meta-analysis was performed when at least three sets of data were available.

In secondary analyses, we examined whether particular subgroups of patients benefited from MBIs. We performed meta-regression analysis with the variables of interest when data were available from five or more of the recruited studies. The clinical variables entered into the meta-regression analysis included age, gender, disengagement early from the study, treatment duration of mindfulness, and Jadad scores.



**Results**

**Studies included in the meta-analysis**

After excluding five studies with mixed populations of patients (e.g. both patients with BD and major depression joined together) (Crane et al., 2008; Garland et al., 2016; Hamilton et al., 2012; Kenny and Williams, 2007; Ramel et al., 2004)(full details in Figure 1 and Supplementary Table 2), 12 articles met the inclusion criteria (Biseul et al., 2016; Bos et al., 2014; Deckersbach et al., 2012; Howells et al., 2014; Ives-Deliperi et al., 2013; Miklowitz et al., 2009; Miklowitz et al., 2015; Perich et al., 2013a; Perich et al., 2013b; Stange et al., 2011; Weber et al., 2010; Williams et al., 2008) (Table 1). The enrolled studies included 274 participants (68.5% female), with a mean age of 41.1 (standard deviation (SD)=10.7) years.

**Among the recruited 12 articles, the study by Perich (2013a) was designed as randomized comparison trial but both of the groups received MBIs with different frequency (Perich et al., 2013a).** Three of the included articles were controlled trials and included 132 participants (mean age = 39.2 (SD 10.3) years, mean proportion of females = 56.2%) (Ives-Deliperi et al., 2013; Perich et al., 2013b; Williams et al., 2008). The remaining nine studies were uncontrolled studies and included 142 participants (mean age = 41.8 (SD=10.8) years, mean proportion of females = 73.7%) (Biseul et al., 2016; Bos et al., 2014; Deckersbach et al., 2012; Howells et al., 2014; Miklowitz et al., 2009; Miklowitz et al., 2015; Perich et al., 2013a; Stange et al., 2011; Weber et al., 2010). The baseline mood characteristics of the participants in these selected studies were euthymic **(defined as a HADS score < 10 and YMRS score <4) (Howells et al., 2014)**, in remission (defined as meeting the DSM-IV-TR or National Institute of Mental Health (NIMH) criteria) (Miklowitz et al., 2009; Williams et al., 2008), or residual depressive or manic symptoms (Biseul et al., 2016; Deckersbach et al., 2012; Ives-Deliperi et al., 2013; Miklowitz et al., 2015; Perich et al., 2013a; Perich et al., 2013b; Stange et al., 2011; Weber et al., 2010) (Supplementary Table 5).

All twelve trials compared changes in the severity of depressive, anxiety, and manic symptoms after MBIs. Of them, 10 used MBCT (Deckersbach et al., 2012; Howells et al., 2014; Ives-Deliperi et al., 2013; Miklowitz et al., 2009; Miklowitz et al., 2015; Perich et al., 2013a; Perich et al., 2013b; Stange et al., 2011; Weber et al., 2010; Williams et al., 2008), one used mindfulness-based relapse prevention (MBRP) (Biseul et al., 2016), and one used mindfulness training (Bos et al., 2014). The duration of mindfulness therapy in these studies was 8 (Biseul et al., 2016; Bos et al., 2014; Howells et al., 2014; Ives-Deliperi et al., 2013; Miklowitz et al., 2009; Miklowitz et al., 2015; Perich et al., 2013a; Perich et al., 2013b; Weber et al., 2010; Williams et

al., 2008) or 12 weeks (Deckersbach et al., 2012; Stange et al., 2011). Six of the studies provided follow-up data (at 1, 3, 6, and 12 months after the MBIs) (Deckersbach et al., 2012; Miklowitz et al., 2015; Perich et al., 2013a; Perich et al., 2013b; Stange et al., 2011; Weber et al., 2010). In this meta-analysis, we used the post-treatment outcome data immediately after the interventions (except for one study which defined re-assessment within 1 week (Weber et al., 2010) and another which defined re-assessment within 1 month (Stange et al., 2011) after the interventions).

**Methodological quality of the included studies**

Similar to previous systematic reviews and meta-analyses of MBCT (Chiesa and Serretti, 2011; Coelho et al., 2007), we assessed the quality of the included studies using the Jadad scale. Across all 12 studies, the average Jadad score was 1.33 with a SD of 0.49 (Supplement Table 3). The average Jadad score in the controlled studies was 1.67 (SD = 0.58) compared to **1.11 (SD = 0.33)** in the uncontrolled studies.

**Meta-analysis investigating the effect of mindfulness-based interventions on the symptom load: pre- to post-test studies**

For symptom load in pre- to post-test studies, MBIs resulted in significant improvements in depressive and anxiety symptoms after the intervention (depressive, k = 7, n = 100, Hedges' $g$ = 0.58, 95% CI = 0.31-0.84, $p < 0.001$; anxiety, k = 4, n = 68, Hedges' $g$ = 0.34, 95% CI = 0.01-0.67, $p$ = 0.043) (Figure 2A and 2B). This significance persisted when focusing on the studies using MBCT only (depressive, k = 6, n = 95, Hedges' $g$ = 0.59, 95% CI = 0.29-0.90, $p< 0.001$; anxiety, k = 4, n = 68, Hedges' $g$ =

0.34, 95% CI = 0.01-0.67, $p$= 0.043). Only one study provided data on changes in depressive symptoms but not anxiety symptoms in patients receiving treatment other than MBCT (they used MBRP), and this study was not included in subgroup meta-analysis (Biseul et al., 2016). In that study, the main changes in depressive symptoms also showed a significant improvement (MADRS from 14.3 +/-11.3 to 4.5 +/- 2.3) (Biseul et al., 2016). However, MBIs did not significantly improve manic symptoms (k = 6, n = 89, Hedges' $g$ = 0.09, 95% CI = -0.16-0.33, $p$ = 0.488) (Figure 2C). In addition, this insignificance persisted after focusing on the studies using MBCT (k = 5, n = 84, Hedges' $g$ = 0.06, 95% CI = -0.20-0.31, $p$ = 0.662). As above, only the study by Biseul provided data on changes in manic symptoms with treatment other than MBCT (they used MBRP) (Biseul et al., 2016), and subgroup meta-analysis was not performed. The main changes in manic symptoms in Biseul`s study did not achieve statistical significance (YMRS from 1.2 +/- 1.3 to 0.3 +/- 0.8) (Biseul et al., 2016).

There was no evidence of significant publication bias in Egger's regression test **with regards to depression** and anxiety but significant publication bias was found in manic symptoms (depressive, t value = 0.31, df = 5, $p$ = 0.77; anxiety, t value = 0.56, df = 2, $p$ = 0.630; mania, t value = 4.15, df = 4, $p$ = 0.014) or heterogeneity (depressive, Q value = 5.62, df = 6, $I^2$ = 0.00, $p$ = 0.467; anxiety, Q value = 1.26, df = 3, $I^2$ = 0.00, $p$ = 0.738; mania, Q value = 1.56, df = 5, $I^2$ = 0.00, $p$ = 0.906).

The meta-analysis results for the primary outcomes are shown in Figure 2.

**Meta-analysis of investigating of the effect of mindfulness-based interventions on symptom load: controlled trials**

For symptom load in the controlled studies, MBIs were not significantly more efficacious than control conditions in improving depressive and anxiety symptoms (depressive, k = 3, n = 132, Hedges' *g* = 0.46, 95% CI = -0.44-1.35, *p* = 0.315; anxiety, k = 3, n = 132, Hedges' *g* = 0.33, 95% CI = -0.84-1.50, *p* = 0.578) (Figure 3A and 3B). For mania, only one study compared MBIs with TAU, and no significant treatment effect was observed (n = 95, baseline YMRS scores MBIs: 4.98 +/- 4.49, Controls: 5.47 +/- 4.36; post-treatment, MBIs: 3.97 +/- 4.57, Controls: 4.44 +/- 4.38, non-significance).

There was no evidence of publication bias in Egger's regression test (depressive, t value = 6.43, df = 1, *p* = 0.098; anxiety, t value = 4.29, df = 1, *p* = 0.146). However, significant heterogeneity was observed both in anxiety symptoms and depressive symptoms (depressive, Q value = 8.07, df = 2, $I^2$ = 75.2, *p* = 0.018; anxiety, Q value = 13.6, df = 2, $I^2$ = 85.3, *p* = 0.001).

**Meta-regression of MBIs symptom load moderators**

No other significant associations were found between the various outcomes (*i.e*. depression and anxiety) and covariates in the uncontrolled studies (supplement table 4).

**Meta-analysis: the effect of mindfulness-based interventions on secondary outcomes**

For the secondary outcomes, comparing changes in baseline to post-treatment scores, MBIs significantly improved mindfulness ability (k = 5, n = 81,

Hedges' *g* = 0.49, 95% CI: 0.12-0.85, *p* = 0.009) and attention (k = 3, n = 43, Hedges' *g* = 0.61, 95% CI: 0.19-1.03, *p* = 0.005) in patients with BD, but not in cognition (k = 3, n = 43, Hedges' *g* = 0.35, 95% CI: -0.15-0.84, *p* = 0.171) (Figure 4A to 4C, scale used in Supplementary Table 5). We could not perform subgroup meta-analyses in the other subdomains of cognition and stress as there were fewer than three relevant articles for each. However, MBIs seemed to improve executive and spatial/verbal memory rather than cognitive flexibility and impulsiveness/distractibility in two trials (Ives-Deliperi et al., 2013; Stange et al., 2011). With regards to the prevention of relapse/recurrence, only two studies (one uncontrolled and one controlled study) considered this as a secondary outcome (Miklowitz et al., 2015; Perich et al., 2013b). Therefore, we could not perform meta-analysis on these data.

**Adverse events and attrition**

Although we tried to investigate potential adverse events associated with the MBIs, none of the enrolled studies reported any adverse event during treatment. Regarding attrition, the rate ranged from 8.2% (Biseul et al., 2016) to 41.7% (Miklowitz et al., 2015). Two studies reported that all participants completed the whole study (Howells et al., 2014; Ives-Deliperi et al., 2013) and another two did not provide data (Bos et al., 2014; Williams et al., 2008).

**Discussion**

The results of this current meta-analysis indicate that patients with BD may experience significant improvements in depressive and anxiety symptoms but not manic symptoms after receiving MBIs, according to endpoint versus baseline severity scores. However, these apparently beneficial effects were derived from uncontrolled trials (pre- to post-test studies), whilst in the few (k=3) included controlled trials, MBIs failed to significantly improve the severity of depressive, anxiety, or manic symptoms. For the secondary outcomes, MBIs seemed to improve attention and mindfulness ability and attention in the patients with BD, again in pre- to post-test analyses. Nevertheless, there were insufficient data to compare MBIs to control conditions for our secondary outcome measures.

To the best of our knowledge, this is the first meta-analysis to specifically focus on the efficacy of adjunctive MBIs in patients with BD and to comprehensively assess distinct outcomes with regards to the symptoms of BD. Overall, the within-group effect sizes were moderate for depressive (0.58) and small for anxiety (0.34), however they were negligible in between-groups analyses. A comprehensive comparison of the main results of the current meta-analysis and previous meta-analyses is summarized in Table 2 (Chiesa and Serretti, 2011; Gotink et al., 2015; Hofmann et al., 2010; Klainin-Yobas et al., 2012; Kuyken et al., 2016; Piet and Hougaard, 2011; Strauss et al., 2014), which showed that our results are consistent with previous reports with regards to the effects of MBIs in the treatment of depressive mood in patients with mental disorders (Chiesa and Serretti, 2011; Klainin-Yobas et al., 2012; Strauss et al., 2014). Similarly, we found significant differences in the severity of anxiety in the pre- and post- analyses. These findings

were all derived from uncontrolled trials, and therefore there is currently a lack of strong evidence supporting the role of MBIs in patients with BD in clinical practice. More controlled studies are needed to better determine the effect of MBIs on mood severity. In particular, future randomized controlled trials (RCTs) are needed to compare the influence of MBIs versus control conditions to rule out a potential non-specific effect in the pre- and post-test analyses. In the three RCTs in our analysis we found no effect on the primary outcomes. **The effect size is quite substantial (Hedges' *g*=0.46 and 0.33 for reducing depression and anxiety, respectively), but the p-value is not significant because of the small sample sizes of three RCTs.** However, three studies are clearly insufficient to make any strong recommendations regarding the potential efficacy of MBIs to improve health outcomes in patients with BD.

The potential mechanism by which mindfulness could reduce symptoms of depression and anxiety might be explained, at least in part, by emotional regulation (Aldao et al., 2010) Major emotional regulation strategies related to mindfulness include reappraisal, rumination, worry, and non-acceptance (Desrosiers et al., 2013). Reappraisal (or reframing) is defined as the attempt to reinterpret an emotion-eliciting experience in a way that alters its emotional impact (Gross and John, 2003). Practicing mindfulness by taking a nonjudgmental stance toward an experience could result in a tendency to adapt a positive reappraisal of a negative event, thereby leading to improvements in depression and anxiety symptoms (Chambers et al., 2009)**.** In addition, mindfulness may attenuate worry and rumination, which are characterized by repetitive thoughts on specifically negative emotions, and lead to focus on future threats characteristic of worry, both of which are central features of depression and anxiety (Desrosiers et al., 2013). However,

**more studies** are needed to validate these hypotheses.

In contrast to the changes in depression and anxiety symptoms, we found a non-significant treatment effect of MBIs on manic symptoms, even when comparing pre- and post-intervention severity scores. Although one article reported that a single patient who did not receive MBRP experienced elevated manic symptoms according to YMRS score (from 0 at baseline to 6 after the intervention) compared to those who did receive MBRP interventions, a definite conclusion cannot be made from a single case (Biseul et al., 2016). A 'floor effect' could partly explain the lack of benefit of MBIs on manic symptoms, because participants with an index (hypo) manic episode were excluded from several trials (Bos et al., 2014; Howells et al., 2014; Miklowitz et al., 2009; Miklowitz et al., 2015; Perich et al., 2013a; Perich et al., 2013b; Williams et al., 2008). However, in real world clinical practice, it could be challenging to engage acute manic participants in MBI-based interventions, because MBIs require participants to be fully aware of current experiences. Therefore, MBIs could be more suitable for the prevention rather than the treatment of manic relapses/recurrence. However, the largest study to date concerning MBIs which included patients with BD as adjunctive MBI to TAU versus TAU alone reported no difference between treatment groups in the prevention of relapse/recurrence rates of either depression or mania/hypomania episodes over a 12-month period (Perich et al., 2013b).

With regards to the secondary outcomes, we did not find that MBIs had beneficial effects on cognition based on pre- and post- test analyses. In addition, not all of these trials reported baseline cognitive status. Therefore, we cannot make any definitive conclusions regarding the role of MBIs on cognition. Nevertheless, our

results suggest the potential of MBIs to enhance attention, a sub-domain of cognition in patients with BD, and future RCTs are warranted to investigate this issue. In addition, MBIs have been shown to improve mindfulness ability (e.g., maintaining a non-judgmental and non-reactive stance toward inner experience) as measured by the five-facet mindfulness questionnaire (FFMQ), Kentucky inventory of mindfulness skills (KIMS), or mindful attention awareness scale (MAAS), and improvements in the severity of depressive and anxiety symptoms may be related to greater mindfulness. Perich et al. reported that more frequently practicing mindfulness (3 times a week or more) resulted in significant improvements in depression and anxiety symptoms supporting this hypothesis. Adherence issues should also be evaluated in the future studies (Perich et al., 2013a).

We did not perform subgroup meta-analysis for several secondary outcomes due to the lack of evidence available (fewer than three independent studies). However, individual studies reported apparently beneficial therapeutic effects for MBIs in some domains such as the quality of life (Bos et al., 2014), well-being (Deckersbach et al., 2012), emotional regulation (Deckersbach et al., 2012; Ives-Deliperi et al., 2013), stress, and rumination (Deckersbach et al., 2012).

**Limitations**

There are several limitations to this study. First, the included trials had a small sample size and often provided no details on randomization procedures. In addition, we only enrolled three controlled studies, of which two used a low-quality control design (such as a waiting list) (Ives-Deliperi et al., 2013; Williams et al., 2008) and the other used a relatively better control design of TAU (applied psychoeducation) (Perich et al., 2013b) as the control group. Usually, MBI sessions can persist for 1 to 2 hours, which greatly increases the time the patients are "taken care of", resulting in moderate effects on their well-being and improvements in depressive and anxiety symptoms. As such, future controlled studies with high-quality comparison groups are needed. Second, the total number of controlled studies recruited in the current meta-analysis was small, precluding the ability to make firm conclusions with practical clinical implications. The findings of the present meta-analysis study were mainly derived from uncontrolled trials, and the average Jadad score was relatively low **(1.25 +/- 0.45)**, which may have influenced the results. Therefore, our findings should be interpreted with caution. Third, it is not uncommon to overestimate the efficacy of both pharmacotherapy and psychological treatment in clinical trials due to publication bias and the selective reporting of 'positive' findings (Driessen et al., 2015; Turner et al., 2008). Even though the interventions were efficacious, they may have been less efficacious than the studies would suggest. Fourth, we may have missed a number of non-English articles focusing on MBIs. Fifth, we could not rule out the possible confounding effects of concurrent psychotropic agents due to limited available data. Some psychological treatments for patients with BD may work partly by increasing medication adherence or changing life style factors resulting in greater regularity (Crowe et al., 2012). In addition, changes in medications may have

occurred throughout the trials, and this may have impacted the results. Sixth, the high rate of disengaging early from the study in some trials (Biseul et al., 2016; Miklowitz et al., 2015) might have contributed to confounding our results. None of the recruited studies applied treatment monitoring to alert the therapists of patients who were at risk of eventual treatment failure, leading to the high disengagement rate. Using adequate treatment monitoring to improve quality control in future RCTs is needed (Tasca et al., 2016).

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**Conclusion**

The current meta-analysis does not support that MBIs can alleviate depressive and anxiety symptoms in patients with BD compared to controls. However, there was some tentative evidence of favorable outcomes in the pre- and post-test studies, although a non-specific effect cannot be ruled out. Hence, the few (k=3) controlled studies did not support the efficacy of MBIs for the treatment of BD. Even though MBIs appeared to be a feasible therapeutic option for patients with BD, the accessibility of MBIs was not strictly assessed by the present meta-analysis and the studies that it included. **Currently, it is not justified to use adjunctive MBIs in the treatment of bipolar disorder.** Future large randomized controlled studies are needed to evaluate their **effectiveness** in various healthcare settings.

**Competing interest:**

The authors state that there are no any competing interests or funding sources in the current literature.

**Role of the Funding source**

The authors stated that there is no any funding source to current study.

**Contributors**

Che-Sheng Chu, the first author, takes the responsibility of writing this manuscript.

Tien-Yu Chen, Chia-Hung Tang, Dian-Jeng Li, Wei-Cheng Yang, and Ching-Kuan Wu contribute hugely in the study design.

Brendon Stubbs and André F. Carvalho, the specialties of meta-analysis, help in the meta-analysis construction.

Eduard Vieta and David J. Miklowitz, the specialties of mindfulness based intervention, take the responsibilities of formation of concept of mindfulness based intervention.

Ping-Tao Tseng and Pao-Yen Lin, the corresponding authors, take all the responsibility of collecting all the information from the other authors, revise the manuscript, and submit the manuscript.

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**Figure 1.** Flowchart of the selection strategy and inclusion/exclusion criteria for the current meta-analysis.

**Figure 2.** (2A) Forest plot showing effect sizes (Hedges' *g*) and 95% confidence intervals (CIs) from the pooled results of pre- to post- treatment comparison of depressive symptoms. (2B) Forest plot showing effect sizes (Hedges' *g*) and 95% confidence intervals (CIs) from the pooled results of pre- to post- treatment comparison of anxiety symptoms. (2C) Forest plot showing effect sizes (Hedges' *g*) and 95% confidence intervals (CIs) from pooled results of pre- to post- treatment comparison of manic symptoms.

**Figure 3.** (3A) Experiment-Control comparison of depressive outcome. Figure (3B) Experiment-Control comparison of anxiety outcome.

**Figure 4.** (4A) Pre- to post- treatment comparison of secondary outcome of mindfulness ability. Figure (4B) Pre- to post- treatment comparison of secondary outcome of attention. Figure (4C) Pre- to post- treatment comparison of secondary outcome of cognition.

Abbreviation: CI: confidence interval



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**Table 1**: summarization of recruited studies in current meta-analysis

| Author (year) | Criteria (Psychiatry) | Diagnosis | Comparison | Subjects | Mean age | Female (%) | Pre-Tx mood severity[1] | Post-Tx mood severity[1] | Drop-out rate (%) | country |
|---|---|---|---|---|---|---|---|---|---|---|

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Biseul, I. (2016) | DSM-IV | BD Substance | Pre-post Tx | 5 | 48.9 | 40.0 | (MADRS) 7.7±6.2 (YMRS) 0.3±0.8 | (MADRS) 4.5±2.3 (YMRS) 1.2±1.3 | 8.2 | France |
| Miklowitz, D. J. (2015) | DSM-IV | Perinatal women with BD | Pre-post Tx | 12 | 33.7 | 100.0 | (BDI-II) 7.7±8.9 (HAMD) 3.14±2.34 (YMRS) 4.1±4.1 (STAI) 43.8±4.8 (FFMQ) 132.5±19.1 | n/a | 41.7 | USA |
| Bos, E. H. (2014) | DSM-IV | BD | Pre-post Tx | 42 | 45.5 | 69.2 | n/a | n/a | n/a | Netherlands |
| Howells, F. M. (2014) | DSM-IV | BD | Pre-post Tx | 12 | 37.0 | 77.8 | *(YMRS) 3.4±3.0 (HADS-A) 8.4±4.5 (HADS-D) 5.1±2.9 | (HADS-A) 7.8±3.5 (HADS-D) 5.8±4.8 | 0.0 | South Africa |
| Ives-Deliperi, V. L. (2013) | DSM-IV | BD | MBI + TAU<br>TAU (waiting list) | 16<br>7 | 37.6 | 60.0 | (HADS-D) 5.8±4.2 6.0±4.8 (BAI) 19.8±12.7 23.0±9.4 | (HADS-D) 4.0±3.1 6.4±4.8 (BAI) 14.1±12.1 20.6±9.9 | 0.0 | South Africa |
| Perich, T. (2013) [a, #] | DSM-IV | BD | MBI + TAU<br>TAU | 48<br>47 | n/a | 65.0<br>66.0 | (MADRS) 11.2±8.2 14.6±10.9 (YMRS) 5.0±4.5 5.5±4.4 (DASS-D) 14.8±12.1 19.5±14.2 (DASS-A) | (MADRS) 7.1±7.3 11.1±9.3 (YMRS) 4.0±4.6 4.4±4.4 (DASS-D) 13.7±11.9 15.7±14.7 (DASS-A) | 37.9 | Australia |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | 11.9±10.4<br>12.9±11.2 | 9.7±9.5<br>5.4±9.1 | | |
| Perich, T. (2013) [b, #] | DSM-IV | BD | Pre-post Tx | 23 | 42.0 | 69.0 | (MADRS) 11.1±8.2<br>(YMRS) 4.8±3.7<br>(DASS-D) 14.4±11.9<br>(DASS-A) 12.2±10.7 | (MADRS) 8.8±7.3<br>(YMRS) 4.5±4.8<br>(DASS-D) 12.2±8.7<br>(DASS-A) 8.8±6.7 | n/a | Australia |
| Deckersbach, T. (2012) | DSM-IV | BD | Pre-post Tx | 12 | 38.7 | 80.0 | (HAMD) 11.8±7.2<br>(YMRS) 5.4±5.1 | (HAMD) 6.3±7.6<br>(YMRS) 4.7±7.1 | 16.7 | USA |
| Stange, J. P. (2011) | DSM-IV | BD | Pre-post Tx | 8 | 41.9 | 75.0 | n/a | n/a | 10.0 | USA |
| Weber, B. (2010) | DSM-IV | BD | Pre-post Tx | 15 | 48.0 (median) | 73.3 | (YMRS) 1 (median)<br>(BDI-II) 10 (median) | *(YMRS) 1 (median)<br>*(BDI-II) 15 (median) | 34.8 | Switzerland |
| Miklowitz, D.J. (2009) | DSM-IV | BD | Pre-post Tx | 22 | 40.6 | 72.7 | (YMRS) 2.1±2.9<br>(BDI) 15.6±12.1<br>(BAI) 15.4±11.4 | (YMRS) 1.8±1.7<br>(BDI) 10.6±7.5<br>(BAI) 12.8±10.9 | 27.3 | UK |
| Williams, J. M. (2008) | DSM-IV | BD | MBI + TAU<br>TAU (waiting list) | 7<br>7 | 36.9<br>46.8 | 71.4<br>28.6 | (BAI) 12.7±12.1<br>11.4±8.5<br>(BDI) 15.8±14.4<br>12.8±8.1 | (BAI) 6.8±5.7<br>20.6±11.3<br>(BDI) 7.1±7.7<br>15.3±8.1 | n/a | UK |

[#]: from same population but different study design.

*: derive effect size from other statistical data.

[1]: as the choice of specific scales for mood severity, we preferred (1) BDI, followed by DASS, MADRS and HAM-D for depressive severity, (2) BAI, followed by DASS and STAI for anxiety severity, and (3) YMRS for manic severity because the most studies using BDI, BAI, and YMRS for depressive, anxiety, and manic severity.

Abbreviation: BAI: Beck anxiety index; BD: bipolar disorder; BDI: Beck depression inventory; CPAS: clinical positive affective scale; DASS: depression anxiety stress scales; DSM-IV: diagnostic and statistical manual of mental disorders, 4th edition; FFMQ: five-facet mindfulness questionnaire; HADS: hospital anxiety and depression scale; HAMD: Hamilton depressive scale; MADRS: Montgomery–Åsberg depression rating scale; MBI: mindfulness-based intervention; n/a: not available; Pre-post Tx: comparison of disease severity before and after treatment; STAI: state-trait anxiety inventory; TAU: treatment as usual; Tx: treatment; YMRS: Young mania rating scale

a. Perich, T., Manicavasagar, V., Mitchell, P.B., Ball, J.R., Hadzi-Pavlovic, D., 2013b. A randomized controlled trial of mindfulness-based cognitive therapy for bipolar disorder. Acta Psychiatr Scand 127, 333-343.
b. Perich, T., Manicavasagar, V., Mitchell, P.B., Ball, J.R., 2013a. The association between meditation practice and treatment outcome in Mindfulness-based Cognitive Therapy for bipolar disorder. Behav Res Ther 51, 338-343.

**Table 2:** Summary and comparison of different findings of meta-analyses by other studies

| Article | Intervention | Diagnosis | Studies (N) | Primary outcome | Secondary | Side effect | Drop out |
|---|---|---|---|---|---|---|---|
| Chu CS (2017) (current MA) | MBIs (MBCT: 10 MBSR: 1 MT: 1) | BD | **12** | Pre MBIs vs post MBIs: More reduced symptoms of: Depression (Hedges' *g*: 0.58, 95% CI: 0.31 to 0.84) | Pre MBIs vs post MBIs: More benefit in: Mindfulness ability (Hedges' *g*: 0.49, 95% CI: 0.12 to 0.85) Attention (Hedges' *g*: 0.61, 95% CI: 0.19 to 1.03) But not in cognition (Hedges' *g*: 0.35, | n/a | 25.7 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | Anxiety (Hedges' *g*: 0.34, 95% CI: 0.01 to 0.67)<br>But Not Mania (Hedges' *g*: 0.09, 95% CI: -0.16 to 0.33)<br>MBIs + TAU vs TAU:<br>No reduced symptoms of Depression (Hedges' *g*: 0.46, 95% CI: -0.44 to 1.35)<br>Anxiety (Hedges' *g*: 0.33, 95% CI: -0.84 to 1.50)<br>Mania (only one study enrolled) | 95% CI: -0.15 to 0.84)<br>MBIs + TAU vs TAU:<br>Not performed due to limited data available (Less than 3 articles in each secondary outcomes) | | |
| MA by Kuyken W (2016) [a] | MBCT | Recurrent MDD | 9 | Reduced risk of depressive 60-weeks relapse<br>MBCT vs No-MBCT (HR: 0.69; 95% CI: 0.58 | n/a | 10 SAE in MBCT<br>16 SAE in non-MBCT | n/a |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | to 0.82) MBCT vs active treatment (HR: 0.79; 95% CI: 0.64 to 0.97) MBCT vs antidepressants (HR: 0.77; 95% CI: 0.60 to 0.98) | | | |
| MA by Gotink RA (2015) [b] | MBIs (MBSR, MBCT) | Physical/mental diseases | 115 | MBSR and MBCT vs wait-list/TAU: More reduced symptoms of: Depression (SMD=-0.37 ;95% CI: -0.45 to -0.28) Anxiety (SMD=-0.48 ;95% CI: -0.56 to -0.40) | MBSR and MBCT vs wait-list/TAU: More reduced symptoms of: Stress(SMD=-0.51;95% CI: -0.67 to -0.36) Quality of life(SMD=-0.39;95% CI: -0.70 to -0.08) Physical functioning(SMD=-0.27;95% CI: -0.42 to -0.12) | n/a | n/a |
| MA by Strauss C (2014) [c] | MBIs (MBSR, MBCT, PBCT) | Depression Anxiety disorder | 12 | MBIs vs control: More reduced symptoms of: Depression (SMD= | n/a | n/a | (median) 15.5 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | -0.73; 95%CI: -1.36 to -0.09) But Not for anxiety (SMD=-0.55 ; 95% CI: -1.18 to 0.09) | | | |
| MA by Klainin-Yobas P (2012) [d] | MBIs (MBSR, MBCT, ABT, DBT, MAGT etc.) | Mental disorder | 39 | MBIs vs TAU: More reduced symptoms of: Depression (SMD=0.53; 95% CI: 0.39 to 0.67) | n/a | n/a | n/a |
| MA by Chiesa A (2011) [e] | MBCT | Mental disorders | 16 | MBCT+TAU vs TAU: Relapse Prevention (OR: 0.30; 95% CI: 0.17 to 0.56) Reduced depress (SMD: -10.3; 95% CI: -17.2 to -3.41) in Depressive disorder Reduced anxiety (SMD: -13.8; 95% | n/a | n/a | n/a |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | CI: -23.2 to -4.42) in patient with BD | | | |
| MA by Piet J (2011)[f] | MBCT | Recurrent MDD | 6 | Reduced risk of depression relapse MBCT vs TAU/placebo (RR: 0.66; 95% CI: 0.53 to 0.82) | n/a | n/a | 16.2 |
| MA by Hofmann SG (2010)[g] | MBIs (MBCT, MBSR, MT, etc.) | Anxiety and depress in physical/mental disease | 44 | Pre MBIs vs post MBIs: Reduced anxiety in various diseases (Hedges' g = 0.63, 95% CI: 0.53 to 0.73) Reduced depress in various diseases (Hedges' g = 0.59, 95% CI: 0.51 to 0.66). | n/a | n/a | n/a |

Abbreviation: ABT: Acceptance-based behavioural therapy; CBT: Cognitive behavioural therapy; CI: confidence interval; DBT: dialectical behaviour therapy for depression; HR: hazard ratio; MA: meta-analysis; MAGT: Mindfulness and Acceptance-based group therapy; MBCT: mindfulness-based cognitive therapy; MBI: mindfulness-based intervention; MBSR: mindfulness-based stress reduction; MDD: major depressive disorder; MT: mindfulness training; n/a: not available; PBCT : Person-based cognitive therapy; RR: risk ratio; SAE: severe adverse event; SAR: severe adverse reaction; SMD: standardized mean difference; TAU: treatment as usual

a. Kuyken W, Warren FC, Taylor RS, et al. Efficacy of Mindfulness-Based Cognitive Therapy in Prevention of Depressive Relapse: An Individual Patient Data Meta-analysis From Randomized Trials. *JAMA psychiatry* 2016;73(6):565-74. doi: 10.1001/jamapsychiatry.2016.0076

b. Gotink RA, Chu P, Busschbach JJ, et al. Standardised mindfulness-based interventions in healthcare: an overview of systematic reviews and meta-analyses of RCTs. *PloS one* 2015;10(4):e0124344. doi: 10.1371/journal.pone.0124344

c. Strauss C, Cavanagh K, Oliver A, et al. Mindfulness-based interventions for people diagnosed with a current episode of an anxiety or depressive disorder: a meta-analysis of randomised controlled trials. *PloS one* 2014;9(4):e96110. doi: 10.1371/journal.pone.0096110

d. Klainin-Yobas P, Cho MA, Creedy D. Efficacy of mindfulness-based interventions on depressive symptoms among people with mental disorders: a meta-analysis. *International journal of nursing studies* 2012;49(1):109-21. doi: 10.1016/j.ijnurstu.2011.08.014

e. Chiesa A, Serretti A. Mindfulness based cognitive therapy for psychiatric disorders: a systematic review and meta-analysis. *Psychiatry research* 2011;187(3):441-53. doi: 10.1016/j.psychres.2010.08.011

f. Piet J, Hougaard E. The effect of mindfulness-based cognitive therapy for prevention of relapse in recurrent major depressive disorder: a systematic review and meta-analysis. *Clinical psychology review* 2011;31(6):1032-40. doi: 10.1016/j.cpr.2011.05.002

g. Hofmann SG, Sawyer AT, Witt AA, et al. The effect of mindfulness-based therapy on anxiety and depression: A meta-analytic review. *Journal of consulting and clinical psychology* 2010;78(2):169-83. doi: 10.1037/a0018555

**Highlight:**

1. Mindfulness-based interventions (MBIs) have shown promise in improving health outcomes in patients with various psychiatric conditions; however, their effect in bipolar disorder is unclear.

2. In pre- and post-test analyses, MBIs appeared to reduce depressive symptoms, the severity of anxiety, and improve attention, although a non-specific effect may have accounted for these results.

3. Compared to controls, MBIs did not reduce depression, anxiety, or mania, although available evidence was limited to only a few studies.

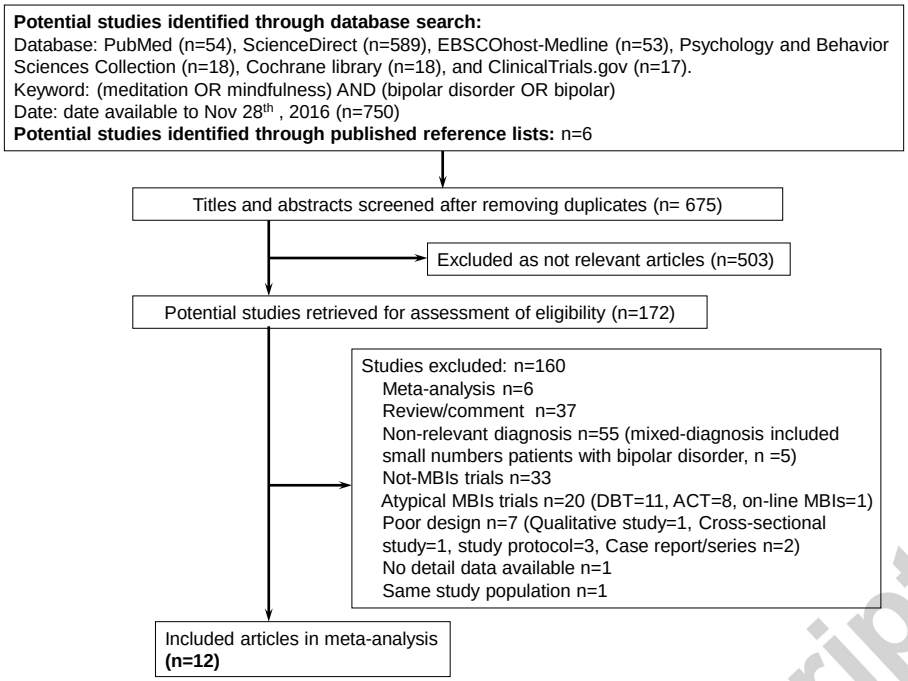


**Figure 1 Search strategy and selection criteria of current study**

| Study name | Hedges's *g* | Lower limit | Upper limit | *p*-Value | Relative weight |
|---|---|---|---|---|---|
| Biseul, I. (2016) | 0.618 | -0.534 | 1.770 | 0.293 | 5.35 |
| Miklowitz, D.J. (2015) | 0.959 | 0.141 | 1.778 | 0.022 | 10.58 |
| Howells, F. M. (2013) | 0.183 | -0.591 | 0.958 | 0.643 | 11.83 |
| Perich, T. (2013) | 0.206 | -0.376 | 0.788 | 0.488 | 20.95 |
| Deckrsbach, T. (2012) | 0.717 | -0.082 | 1.516 | 0.079 | 11.12 |
| Miklowitz, D.J. (2009) | 0.487 | -0.103 | 1.076 | 0.106 | 20.44 |
| Weber, B. (2010) | 1.011 | 0.411 | 1.611 | 0.001 | 19.72 |
| **Overall** | **0.578** | **0.312** | **0.844** | **0.000** | **100.00** |

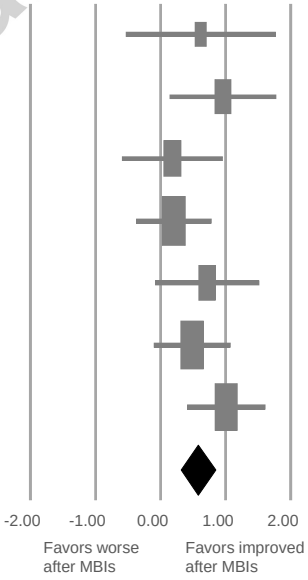


Figure 2A Pre- to post- treatment comparison of depressive symptoms

| Study name | Hedges's *g* | Lower limit | Upper limit | *p*-Value | Relative weight |
|---|---|---|---|---|---|
| Ives-Deliperi, V. L. (2013) | 0.578 | -0.294 | 1.450 | 0.194 | 31.61 |
| Perich, T. (2013) | -0.198 | -0.598 | 0.202 | 0.333 | 41.52 |
| Williams, J.M.G. (2008) | 1.327 | 0.230 | 2.424 | 0.018 | 26.88 |
| **Overall** | **0.457** | **-0.435** | **1.349** | **0.315** | **100.00** |

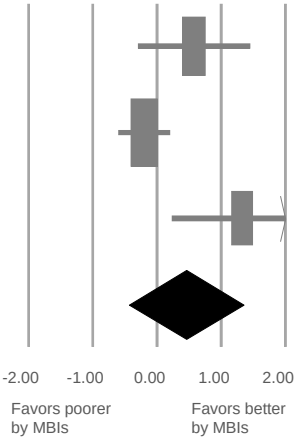


Figure 3A Experiment-Control comparison of depressive outcome

| Study name | Hedges's *g* | Lower limit | Upper limit | *p*-Value | Relative weight |
|---|---|---|---|---|---|
| Bos, E. H. (2014) | 0.525 | -0.184 | 1.234 | 0.146 | 17.57 |
| Perich, T. (2013) | 0.543 | -0.036 | 1.122 | 0.066 | 22.61 |
| Deckrsbach, T. (2012) | 0.593 | -0.198 | 1.383 | 0.142 | 15.11 |
| Weber, B. (2010) | 0.000 | -0.478 | 0.478 | 1.000 | 27.64 |
| Lves-Deliperi, V. L. (2013) | 1.068 | 0.344 | 1.793 | 0.004 | 17.07 |
| **Overall** | **0.487** | **0.124** | **0.850** | **0.009** | **100.00** |

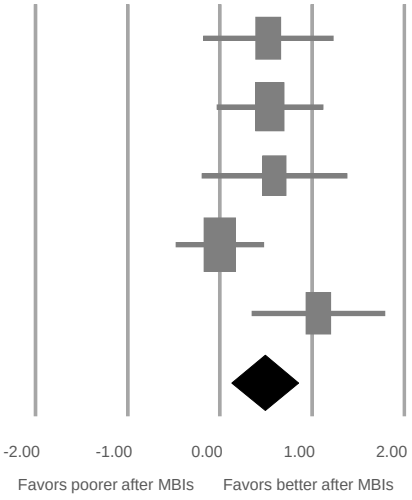


Figure 4A Pre- to post- treatment comparison of secondary outcome of mindfulness ability